E 6560-50-P

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[EPA-HQ-OPP-2021-0274; FRL-10822-01-OCSPP]

Acetophenone; Exemption From the Requirement of a Tolerance

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This regulation establishes an exemption from the requirement of a tolerance for residues of acetophenone when used as an inert ingredient (solvent or co-solvent) in pesticide formulations applied to growing crops. ADAMA Makhteshim Ltd. submitted a petition to EPA under the Federal Food, Drug, and Cosmetic Act (FFDCA), requesting the establishment of this exemption from the requirement of a tolerance. This regulation eliminates the need to establish a maximum permissible level for residues of acetophenone, when used in accordance with the terms of that exemption.

DATES: This regulation is effective [INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. Objections and requests for hearings must be received on or before [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*], and must be filed in accordance with the instructions provided in 40 CFR part 178 (see also Unit I.C. of the **SUPPLEMENTARY INFORMATION**).

ADDRESSES: The docket for this action, identified by docket identification (ID) number EPA-HQ-OPP-2021-0274, is available at *https://www.regulations.gov* or at the Office of Pesticide Programs Regulatory Public Docket (OPP Docket) in the Environmental Protection Agency Docket Center (EPA/DC), West William Jefferson Clinton Bldg., Rm. 3334, 1301 Constitution Ave., NW., Washington, DC 20460-0001. The Public Reading Room is open from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays. The telephone number for the Public Reading Room and the OPP docket is (202) 566-1744. For the latest status information on

EPA/DC services, docket access, visit *https://www.epa.gov/dockets.*

FOR FURTHER INFORMATION CONTACT: Daniel Rosenblatt, Registration Division (7505P), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001; main telephone number: (202) 566-2875; email address: *RDFRNotices@epa.gov*.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this action apply to me?

You may be potentially affected by this action if you are an agricultural producer, food manufacturer, or pesticide manufacturer. The following list of North American Industrial Classification System (NAICS) codes is not intended to be exhaustive, but rather provides a guide to help readers determine whether this document applies to them. Potentially affected entities may include:

- Crop production (NAICS code 111).
- Animal production (NAICS code 112).
- Food manufacturing (NAICS code 311).
- Pesticide manufacturing (NAICS code 32532).

B. How can I get electronic access to other related information?

You may access a frequently updated electronic version of 40 CFR part 180 through the Office of the Federal Register's e-CFR site at *https://www.ecfr.gov/current/title-40.*

C. How can I file an objection or hearing request?

Under FFDCA section 408(g), 21 U.S.C. 346a, any person may file an objection to any aspect of this regulation and may also request a hearing on those objections. You must file your objection or request a hearing on this regulation in accordance with the instructions provided in 40 CFR part 178. To ensure proper receipt by EPA, you must identify docket ID number EPA-HQ-OPP-2021-0274 in the subject line on the first page of your submission. All objections and

requests for a hearing must be in writing and must be received by the Hearing Clerk on or before [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. Addresses for mail and hand delivery of objections and hearing requests are provided in 40 CFR 178.25(b).

In addition to filing an objection or hearing request with the Hearing Clerk as described in 40 CFR part 178, please submit a copy of the filing (excluding any Confidential Business Information (CBI)) for inclusion in the public docket. Information not marked confidential pursuant to 40 CFR part 2 may be disclosed publicly by EPA without prior notice. Submit the non-CBI copy of your objection or hearing request, identified by docket ID number EPA-HQ-OPP-2021-0274, by one of the following methods:

• *Federal eRulemaking Portal*: *https://www.regulations.gov*. Follow the online instructions for submitting comments. Do not submit electronically any information you consider to be CBI or other information whose disclosure is restricted by statute.

• *Mail*: OPP Docket, Environmental Protection Agency Docket Center (EPA/DC), (28221T), 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001.

• *Hand Delivery*: To make special arrangements for hand delivery or delivery of boxed information, please follow the instructions at *https://www.epa.gov/dockets/where-send-comments-epa-dockets#express*.

Additional instructions on commenting or visiting the docket, along with more information about dockets generally, is available at *https://www.epa.gov/dockets*.

II. Petition for Exemption

In the *Federal Register* of June 1, 2021 (86 FR 29229) (FRL-10023-95), EPA issued a document pursuant to FFDCA section 408, 21 U.S.C. 346a, announcing the filing of a pesticide petition (PP IN-11493) by ADAMA Makhteshim Ltd., 3120 Highwoods Blvd., Suite 100, Raleigh, NC 27604. The petition requested that the existing exemption in 40 CFR 180.920 for residues of acetophenone (CAS Reg. No. 98-86-2) be amended to include additional uses for

acetophenone as a solvent or co-solvent inert ingredient in pesticide formulations applied to growing crops. That document referenced a summary of the petition prepared by ADAMA Makhteshim Ltd., the petitioner, which is available in the docket, *https://www.regulations.gov*. There were no comments received in response to the notice of filing.

III. Inert Ingredient Definition

Inert ingredients are all ingredients that are not active ingredients as defined in 40 CFR 153.125 and include, but are not limited to, the following types of ingredients (except when they have a pesticidal efficacy of their own): Solvents such as alcohols and hydrocarbons; surfactants such as polyoxyethylene polymers and fatty acids; carriers such as clay and diatomaceous earth; thickeners such as carrageenan and modified cellulose; wetting, spreading, and dispersing agents; propellants in aerosol dispensers; microencapsulating agents; and emulsifiers. The term "inert" is not intended to imply nontoxicity; the ingredient may or may not be chemically active. Generally, EPA has exempted inert ingredients from the requirement of a tolerance based on the low toxicity of the individual inert ingredients.

IV. Aggregate Risk Assessment and Determination of Safety

Section 408(c)(2)(A)(i) of FFDCA allows EPA to establish an exemption from the requirement for a tolerance (the legal limit for a pesticide chemical residue in or on a food) only if EPA determines that the tolerance is "safe." Section 408(c)(2)(A)(ii) of FFDCA defines "safe" to mean that "there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information." This includes exposure through drinking water and in residential settings but does not include occupational exposure. When making a safety determination for an exemption for the requirement of a tolerance FFDCA section 408(c)(2)(B) directs EPA to consider the considerations in section 408(b)(2)(C) and (D). Section 408(b)(2)(C) of FFDCA requires EPA to give special consideration to exposure of infants and children to the pesticide chemical residue in establishing a tolerance and to "ensure that there is a reasonable

certainty that no harm will result to infants and children from aggregate exposure to the pesticide chemical residue....” Section 408(b)(2)(D) lists other factors for EPA consideration making safety determinations, *e.g.*, the validity, completeness, and reliability of available data, nature of toxic effects, available information concerning the cumulative effects of the pesticide chemical and other substances with a common mechanism of toxicity, and available information concerning aggregate exposure levels to the pesticide chemical and other related substances, among others.

EPA establishes exemptions from the requirement of a tolerance only in those cases where it can be clearly demonstrated that the risks from aggregate exposure to pesticide chemical residues under reasonably foreseeable circumstances will pose no harm to human health. In order to determine the risks from aggregate exposure to pesticide inert ingredients, the Agency considers the toxicity of the inert in conjunction with possible exposure to residues of the inert ingredient through food, drinking water, and through other exposures that occur as a result of pesticide use in residential settings. If EPA is able to determine that a finite tolerance is not necessary to ensure that there is a reasonable certainty that no harm will result from aggregate exposure to the inert ingredient, an exemption from the requirement of a tolerance may be established.

Consistent with FFDCA section 408(c)(2)(A), and the factors specified in FFDCA section 408(c)(2)(B), EPA has reviewed the available scientific data and other relevant information in support of this action. EPA has sufficient data to assess the hazards of and to make a determination on aggregate exposure for acetophenone including exposure resulting from the exemption established by this action. EPA's assessment of exposures and risks associated with acetophenone follows.

A. Toxicological Profile

EPA has evaluated the available toxicity data and considered their validity, completeness, and reliability as well as the relationship of the results of the studies to human risk. EPA has also

considered available information concerning the variability of the sensitivities of major identifiable subgroups of consumers, including infants and children. Specific information on the studies received and the nature of the adverse effects caused by acetophenone as well as the no-observed-adverse-effect-level (NOAEL) and the lowest-observed-adverse-effect-level (LOAEL) from the toxicity studies are discussed in this unit.

Available acute studies on acetophenone show moderate oral and low dermal toxicity. An inhalation toxicity study showed moderate inhalation toxicity. Acetophenone was shown to be a mild irritant to the skin and a severe eye irritant but was not reported to be a dermal sensitizer.

Several repeat dose oral studies (*i.e.*, a 17-week dietary toxicity study in rats, a 90-day gavage study in rats, two developmental toxicity studies in rats and rabbits and a repeat dose toxicity test combined with a reproductive/developmental screening test in rats) have been conducted with acetophenone. The most sensitive effect in the acetophenone database is decreased body weight, which was observed starting at 300 mg/kg/day in a developmental gavage study in rats and at 500 mg/kg/day in the 90-day gavage study in rats.

B. Toxicological Points of Departure/Levels of Concern

Once a pesticide's toxicological profile is determined, EPA identifies toxicological points of departure (POD) and levels of concern to use in evaluating the risk posed by human exposure to the pesticide. For hazards that have a threshold below which there is no appreciable risk, the toxicological POD is used as the basis for derivation of reference values for risk assessment. PODs are developed based on a careful analysis of the doses in each toxicological study to determine the dose at which no adverse effects are observed (the NOAEL) and the lowest dose at which adverse effects of concern are identified (the LOAEL). Uncertainty/safety factors are used in conjunction with the POD to calculate a safe exposure level - generally referred to as a population-adjusted dose (PAD) or a reference dose (RfD) - and a safe margin of exposure (MOE). For non-threshold risks, the Agency assumes that any amount of exposure will lead to some degree of risk. Thus, the Agency estimates risk in terms of the probability of an occurrence

of the adverse effect expected in a lifetime. For more information on the general principles EPA uses in risk characterization and a complete description of the risk assessment process, see *https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/overview-risk-assessment-pesticide-program*.

No effects attributed to a single exposure were seen in the studies provided and therefore, a point of departure (POD) for acute dietary risk was not determined. The most sensitive effect in the acetophenone database is decreased body weight, which was observed starting at 300 mg/kg/day in a developmental gavage study in rats and at 500 mg/kg/day in the 90-day gavage study in rats. Therefore, both studies are considered co-critical. The chronic dietary, incidental oral, dermal and inhalation endpoints are selected from the NOAEL of 250 mg/kg/day based on body weight changes observed starting at 300 mg/kg/day in rats.

C. Exposure Assessment

1. *Dietary exposure from food and feed uses*. In evaluating dietary exposure to acetophenone, EPA considered exposure under the proposed exemption from the requirement of a tolerance. EPA assessed dietary exposures from acetophenone in food as follows:

Because no acute endpoint of concern was identified, a quantitative acute dietary exposure assessment is unnecessary. In conducting the chronic dietary exposure assessment using the Dietary Exposure Evaluation Model DEEM– FCID™, Version 4.02, EPA used food consumption information from the U.S. Department of Agriculture's National Health and Nutrition Examination Survey, What we eat in America, (NHANES/WWEIA). This dietary survey was conducted from 2005 to 2010. The Inert Dietary Exposure Evaluation Model (I–DEEM) is a highly conservative model with the assumption that the residue level of the inert ingredient would be no higher than the highest tolerance for a given commodity. Implicit in this assumption is that there would be similar rates of degradation between the active and inert ingredient (if any) and that the concentration of inert ingredient in the scenarios leading to these highest of tolerances would be no higher than the concentration of the active ingredient. The

model assumes 100 percent crop treated (PCT) for all crops and that every food eaten by a person each day has tolerance-level residues. A complete description of the general approach taken to assess inert ingredient risks in the absence of residue data is contained in the memorandum entitled ‘‘Update to D361707: Dietary Exposure and Risk Assessments for the Inerts.’’ (12/21/2021) and can be found at *https://www.regulations.gov* in docket ID number EPA-HQ-OPP-2018-0090-0002.

2. *Dietary exposure from drinking water*. For the purpose of the screening level dietary risk assessment to support this request for an exemption from the requirement of a tolerance for acetophenone, a conservative drinking water concentration value of 100 ppb based on screening level modeling was used to assess the contribution to drinking water for the chronic dietary risk assessments for parent compound. These values were directly entered into the dietary exposure model.

3. *From non-dietary exposure*. The term “residential exposure” is used in this document to refer to non-occupational, non-dietary exposure (*e.g.*, textiles (clothing and diapers), carpets, swimming pools, and hard surface disinfection on walls, floors, tables). Based on the pesticide product labels reviewed, in a conservative effort to assess exposure, the EPA has conducted a screening level assessment using high-end exposure scenarios for pesticidal use on lawns/turf and antimicrobial cleaning products.

Risks were calculated using the Margin of Exposure (MOE) approach. This is a ratio of the body burden to the toxicological Point of Departure (POD). A MOE greater than 100 indicates that the exposure scenario does not demonstrate a risk of concern for acetophenone. For all residential handler and post- application scenarios, for both adults and children, for application of pesticides containing this inert ingredient to lawns and turf and use in cleaning produces, the MOEs were greater than 100 and therefore, there is no risk of concern.

4. *Cumulative effects from substances with a common mechanism of toxicity*. Section 408(b)(2)(D)(v) of FFDCA requires that, when considering whether to establish, modify, or

revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity."

EPA has not found acetophenone to share a common mechanism of toxicity with any other substances, and acetophenone does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has assumed that acetophenone does not have a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see EPA's website at *https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/cumulative-assessment-risk-pesticides*.

D. Safety Factor for Infants and Children

1. *In general*. Section 408(b)(2)(C) of FFDCA provides that EPA shall apply an additional tenfold (10X) margin of safety for infants and children in the case of threshold effects to account for prenatal and postnatal toxicity and the completeness of the database on toxicity and exposure unless EPA determines based on reliable data that a different margin of safety will be safe for infants and children. This additional margin of safety is commonly referred to as the Food Quality Protection Act (FQPA) Safety Factor (SF). In applying this provision, EPA either retains the default value of 10X, or uses a different additional safety factor when reliable data available to EPA support the choice of a different factor.

2. *Prenatal and postnatal sensitivity*. No evidence of offspring susceptibility was observed in the available developmental studies in rats and rabbits or the reproductive/developmental toxicity study in rats. The offspring effects observed in all three studies occurred only in the presence of maternal toxicity.

3. *Conclusion*. EPA has determined that reliable data show the safety of infants and children would be adequately protected if the FQPA SF were reduced from 10X to 1X. That

decision is based on the following findings:

i. The toxicity database for acetophenone is complete.

ii. Acetophenone is a known hypnotic. Clinical signs of neurotoxicity were observed in the available studies. However, these effects were seen at the same or higher doses than the body weight changes. Therefore, the POD is protective of any potential neurotoxicity effects.

iii. There is no evidence that acetophenone results in increased susceptibility in *in utero* rats or rabbits in the prenatal developmental studies or in young rats in the 2-generation reproduction study.

iv. There are no residual uncertainties identified in the exposure databases. The dietary food exposure assessments were performed based on 100% CT and tolerance-level residues. EPA made conservative (protective) assumptions in the ground and surface water modeling used to assess exposure to acetophenone in drinking water. EPA used similarly conservative assumptions to assess post-application exposure of children as well as incidental oral exposure of toddlers. These assessments will not underestimate the exposure and risks posed by acetophenone.

E. Aggregate Risks and Determination of Safety

EPA determines whether acute and chronic dietary pesticide exposures are safe by comparing aggregate exposure estimates to the acute PAD (aPAD) and chronic PAD (cPAD). For linear cancer risks, EPA calculates the lifetime probability of acquiring cancer given the estimated aggregate exposure. Short-, intermediate-, and chronic-term risks are evaluated by comparing the estimated aggregate food, water, and residential exposure to the appropriate PODs to ensure that an adequate MOE exists.

1. *Acute risk*. An acute aggregate risk assessment takes into account acute exposure estimates from dietary consumption of food and drinking water. No adverse effect resulting from a single oral exposure was identified and no acute dietary endpoint was selected. Therefore, acetophenone is not expected to pose an acute risk.

2. *Chronic risk.* Using the exposure assumptions described in this unit for chronic exposure, EPA has concluded that chronic exposure to acetophenone from food and water will utilize 41.2 % of the cPAD for children 1 to 2 years old, the population group receiving the greatest exposure. Based on the explanation in this unit, regarding residential use patterns, chronic residential exposure to residues of acetophenone is not expected.

3. *Short-term risk.* Short-term aggregate exposure takes into account short-term residential exposure plus chronic exposure to food and water (considered to be a background exposure level). Acetophenone is currently used as an inert ingredient in pesticide products that are registered for uses that could result in short-term residential exposure, and the Agency has determined that it is appropriate to aggregate chronic exposure through food and water with short-term residential exposures to acetophenone.

Using the exposure assumptions described in this unit for short-term exposures, EPA has concluded the combined short-term food, water, and residential exposures result in aggregate MOEs of 120 for adults and 110 for children 1 to 2 years old. These MOEs are not of concern because EPA's level of concern for acetophenone is a MOE of 100 or below.

4. *Intermediate-term risk*. Intermediate-term aggregate exposure takes into account intermediate-term residential exposure plus chronic exposure to food and water (considered to be a background exposure level). An intermediate-term adverse effect was identified; however, acetophenone is not currently used as an inert ingredient in pesticide products that are registered for any use patterns that would result in intermediate-term residential exposure. Intermediate-term risk is assessed based on intermediate-term residential exposure plus chronic dietary exposure. Because there is no intermediate-term residential exposure and chronic dietary exposure has already been assessed under the appropriately protective cPAD (which is at least as protective as the POD used to assess intermediate-term risk), no further assessment of intermediate-term risk is necessary, and EPA relies on the chronic dietary risk assessment for evaluating intermediate-term risk for acetophenone.

5. *Aggregate cancer risk for U.S. population*. Based on the lack of structural alerts for carcinogenicity coupled with the result from the studies indicating low concern for mutagenicity, there is low concern for carcinogenicity with acetophenone. Therefore, acetophenone is not expected to pose a cancer risk to humans.

6. *Determination of safety*. Based on these risk assessments, EPA concludes that there is a reasonable certainty that no harm will result to the general population, or to infants and children from aggregate exposure to acetophenone residues.

V. Analytical Enforcement Methodology

An analytical method is not required for enforcement purposes since the Agency is establishing an exemption from the requirement of a tolerance without any numerical limitation.

VI. Conclusions

Therefore, an exemption from the requirement of a tolerance established under 40 CFR 180.920 for acetophenone (CAS Reg. No. 98-86-2) can be amended to include the use as an inert ingredient (solvent or co-solvent) in pesticide formulations applied pre-harvest to growing crops only.

VII. Statutory and Executive Order Reviews

This action establishes an exemption from the tolerance requirement under FFDCA section 408(d) in response to a petition submitted to the Agency. The Office of Management and Budget (OMB) has exempted these types of actions from review under Executive Order 12866, entitled "Regulatory Planning and Review" (58 FR 51735, October 4, 1993). Because this action has been exempted from review under Executive Order 12866, this action is not subject to Executive Order 13211, entitled "Actions Concerning Regulations That Significantly Affect Energy Supply, Distribution, or Use" (66 FR 28355, May 22, 2001), or Executive Order 13045, entitled "Protection of Children from Environmental Health Risks and Safety Risks" (62 FR 19885, April 23, 1997). This action does not contain any information collections subject to OMB approval under the Paperwork Reduction Act (PRA) (44 U.S.C. 3501 *et seq*.), nor does it require

any special considerations under Executive Order 12898, entitled "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations" (59 FR 7629, February 16, 1994).

Since tolerances and exemptions that are established on the basis of a petition under FFDCA section 408(d), such as the tolerance in this final rule, do not require the issuance of a proposed rule, the requirements of the Regulatory Flexibility Act (RFA) (5 U.S.C. 601 *et seq*.), do not apply.

This action directly regulates growers, food processors, food handlers, and food retailers, not States or Tribes, nor does this action alter the relationships or distribution of power and responsibilities established by Congress in the preemption provisions of FFDCA section 408(n)(4). As such, the Agency has determined that this action will not have a substantial direct effect on States or Tribal Governments, on the relationship between the National Government and the States or Tribal Governments, or on the distribution of power and responsibilities among the various levels of government or between the Federal Government and Indian Tribes. Thus, the Agency has determined that Executive Order 13132, entitled "Federalism" (64 FR 43255, August 10, 1999), and Executive Order 13175, entitled "Consultation and Coordination with Indian Tribal Governments" (65 FR 67249, November 9, 2000), do not apply to this action. In addition, this action does not impose any enforceable duty or contain any unfunded mandate as described under Title II of the Unfunded Mandates Reform Act (UMRA) (2 U.S.C. 1501 *et seq*.).

This action does not involve any technical standards that would require Agency consideration of voluntary consensus standards pursuant to section 12(d) of the National Technology Transfer and Advancement Act (NTTAA) (15 U.S.C. 272 note).

VIII. Congressional Review Act

Pursuant to the Congressional Review Act (5 U.S.C. 801 *et seq*.), EPA will submit a report containing this rule and other required information to the U.S. Senate, the U.S. House of Representatives, and the Comptroller General of the United States prior to publication of the rule

in the *Federal Register*. This action is not a "major rule" as defined by 5 U.S.C. 804(2).

List of Subjects in 40 CFR Part 180

Environmental protection, Administrative practice and procedure, Agricultural commodities, Pesticides and pests, Reporting and recordkeeping requirements.

Dated: March 31, 2023.

Daniel Rosenblatt,

Acting Director, Registration Division, Office of Pesticide Programs.

Therefore, for the reasons stated in the preamble, EPA is amending 40 CFR chapter I as follows:

PART 180--TOLERANCES AND EXEMPTIONS FOR PESTICIDE CHEMICAL RESIDUES IN FOOD

1. The authority citation for part 180 continues to read as follows:

Authority: 21 U.S.C. 321(q), 346a and 371.

2. In § 180.920, amend table 1 to 180.920, by revising the entry for "Acetophenone" to read as follows:

§ 180.920 Inert ingredients used pre-harvest; exemptions from the requirement of a tolerance.

* * * * *

Table 1 to 180.920

Inert ingredients	Limits	Uses
* * *	* *	* *
Acetophenone (CAS Reg. No. 98-86-2)		Attractant, solvent, co-solvent
* * *	* *	* *

[FR Doc. 2023-07459 Filed: 4/7/2023 8:45 am; Publication Date: 4/10/2023]